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**UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA**

NEUROGRAFIX, a California corporation;
WASHINGTON RESEARCH
FOUNDATION, a not-for-profit Washington
corporation,
Plaintiffs,
vs.
SIEMENS MEDICAL SOLUTIONS USA,
INC., a Delaware corporation; and
SIEMENS AKTIENGESELLSCHAFT, a
German corporation,
Defendants.

CASE NO. CV 10-1990 MRP(RZX)

**MEMORANDUM IN SUPPORT
OF SIEMENS' MOTION FOR
PARTIAL SUMMARY
JUDGMENT OF INVALIDITY
BASED ON INDEFINITENESS
OF "CONSPICUITY" IN CLAIMS
1, 3, 7, 11, 12, 18, AND THEIR
ASSERTED DEPENDENT
CLAIMS IN U.S. PATENT NO.
5,560,360**

**The Hon. Mariana R. Pfaelzer
United States District Court Judge**

Mem. in Support of Siemens' Mot. for Partial SJ of Indefiniteness

1
2 SIEMENS MEDICAL SOLUTIONS USA,
3 INC.
4 Counterclaim Plaintiff,
5 vs.
6 NEUROGRAFIX, and WASHINGTON
7 RESEARCH FOUNDATION,
8 Counterclaim Defendants.

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8 <i>Amgen, Inc. v. Chugai Pharm. Co.</i> , 9 927 F.2d 1200 (Fed. Cir. 1991)	10 6
10 <i>Arcade Inc. v. 3M Co.</i> , 11 24 U.S.P.Q.2d 1578 (E.D. Tenn. 1991).....	12 8
11 <i>Baldwin Graphic Sys., Inc. v. Siebert, Inc.</i> , 12 2008 WL 4083145 (N.D. Ill. Aug. 27, 2008)	13 15, 17
12 <i>Datamize, LLC v. Plumtree Software, Inc.</i> , 13 417 F.3d 1342 (Fed. Cir. 2005)	14 5, 14, 16
13 <i>Duplan Corp. v. Deering Milliken, Inc.</i> , 14 444 F. Supp. 648 (D. S.C. 1977), <i>aff'd in part,</i> 15 <i>rev'd in part on other grounds</i> , 594 F.2d 979 (4th Cir. 1979)	16 17
14 <i>Exxon Research & Eng'g Co. v. United States</i> , 15 265 F.3d 1371 (Fed. Cir. 2001)	16 5
15 <i>Geneva Pharms., Inc. v. Glaxosmithkline PLC</i> , 16 349 F.3d 1373 (Fed. Cir. 2003)	17 2, 6, 17
16 <i>Halliburton Energy Servs., Inc. v. M-I LLC</i> , 17 514 F.3d 1244 (Fed. Cir. 2008)	18 5, 6
17 <i>Honeywell Int'l, Inc. v. Int'l Trade Comm'n</i> , 18 341 F.3d 1332 (Fed. Cir. 2003)	19 11, 14
18 <i>In re Frederiksen</i> , 19 213 F.2d 547 (C.C.P.A 1954)	20 9, 11
19 <i>Morton Int'l, Inc. v. Cardinal Chem. Co.</i> , 20 5 F.3d 1464 (Fed. Cir. 1993)	21 5, 6, 17
20 <i>S.O.I.TEC Silicon On Insulator Techs. v. MEMC Elec. Materials, Inc.</i> , 21 745 F. Supp. 2d 489 (D. Del. 2010).....	22 9
21 <i>Union Pac. Res. Co. v. Chesapeake Energy Corp.</i> , 22 236 F.3d 684 (Fed. Cir. 2001)	23 8

23 **Statutes**
24

25 35 U.S.C. §112, ¶2	26 1, 3
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2 EXHIBIT LIST
3

4 The following exhibits cited herein refer to the exhibits to the Declaration of
5 Sean M. McEldowney In Support of Siemens' Notice of Motion and Motion for
6 Partial Summary Judgment of Invalidity Based on Indefiniteness of "Conspicuity" in
7 Claims 1, 3, 7, 11, 12, 18, and Their Asserted Dependent Claims in U.S. Patent No.
8 5,560,360, filed concurrently herewith. References to the File History for U.S. Patent
9 No. 5,560,360 are cited as "JA__" and refer to the parties Joint Appendix submitted
10 on February 11, 2011 (D.I. 102).

- 11 **Exhibit IND1:** Excerpts from the deposition of Michael N. Brant-Zawadzki,
12 M.D., dated August 16, 2011
- 13 **Exhibit IND2:** Opening expert report of R. Nick Bryan, M.D., dated July
14 22, 2011
- 15 **Exhibit IND3:** Rebuttal expert report of R. Nick Bryan, M.D., dated August
16 8, 2011
- 17 **Exhibit IND4:** Exhibit C to the opening expert report of Michael E.
18 Moseley, Ph.D., dated January 24, 2011
- 19 **Exhibit IND5:** Exhibit A to the rebuttal expert report of Aaron G. Filler,
20 M.D., dated February 1, 2011
- 21 **Exhibit IND6:** Excerpts from the rebuttal expert report of Aaron G. Filler,
22 M.D., dated February 1, 2011
- 23 **Exhibit IND7:** Excerpts from *Markman* Hearing dated March 24, 2011
- 24 **Exhibit IND8:** S. Bisdas et al., *Reproducibility, Interrater Agreement, and
Age-Related Changes of Fractional Anisotropy Measures at 3T in Healthy Subjects: Effect of the Applied b-Value*, 29
Am. J. Neuroradiology 1128 (2008); NEURO00036251-256
- 25 **Exhibit IND9:** D. Bonekamp et al., *Diffusion Tensor Imaging in Children
and Adolescents: Reproducibility, Hemispheric, and Age-
Related Differences*, NIH Author Manuscript (34
Neuroimage 733) (2007); NEURO00036257-276
- 26 **Exhibit IND10:** R. Boellaard et al., *Effects of Noise, Image Resolution, and
ROI Definition on the Accuracy of Standard Uptake Values:
A Simulation Study*, 45 J. Nuclear Med. 1519 (2004)
- 27 **Exhibit IND11:** N.C. Krak et al., *Effects of ROI Definition and
Reconstruction Method on Quantitative Outcome and
Applicability in a Response Monitoring Trial*, 32 Eur. J.
Nuclear Med. & Molecular Imaging 294 (2005)
- 28 **Exhibit IND12:** Exhibit C to the opening expert report of R. Nick Bryan,
M.D., dated July 22, 2011

1 **Exhibit IND13:** L.P. Clarke et al., *MRI: Stability of Three Supervised*
2 *Segmentation Techniques*, 11 Magnetic Resonance Imaging
3 95 (1993); NEURO00036277-288

4 **Exhibit IND14:** E. Jackson et al., *Accuracy and Reproducibility in*
5 *Volumetric Analysis of Multiple Sclerosis Lesions*, 17 J.
6 Computer Assisted Tomography 200 (1993);
7 NEURO00036289-294

8 **Exhibit IND15:** A. Ozturk et al., *Regional Differences in Diffusion Tensor*
9 *Imaging Measurements: Assessment of Intrarater and*
10 *Interrater Variability*, 29 Am. J. Neuroradiology 1124
11 (2008); NEURO00036324-327

12 **Exhibit IND16:** Excerpts from the opening expert report of Michael E.
13 Moseley, Ph.D., dated January 24, 2011

14 **Exhibit IND17:** Exhibit 2 to the rebuttal expert report of R. Nick Bryan,
15 M.D., dated August 8, 2011

MEMORANDUM OF POINTS AND AUTHORITIES

The Court's claim construction order raised two questions regarding the definiteness of the "conspicuity" term that is incorporated in method claims 1 through 35 of U.S. Patent No. 5,560,360:

- (1) Do persons of skill in the art “agree[] on a method of making [region of interest] selections” for purposes of measuring conspicuity in a magnetic resonance image?
 - (2) Do differences in region of interest selection mean “infringement would depend on who makes the [conspicuity] measurement”?

(D.I. 114 at 14-15.) Testimony from the parties' experts on these questions, as well as literature in the field, confirms that the "conspicuity" term is fatally indefinite under 35 U.S.C. §112, ¶2.

On the first question, Plaintiffs’ own expert admits that “there’s no industry standard one way of” selecting regions of interest (“ROIs”), and that the ‘360 patent does not provide “one standard way” to determine ROIs. (Ex. IND1, Brant-Zawadzki Dep. Tr. at 126:17-127:7; 127:18-128:3.)¹ Rather, Plaintiffs’ expert concedes that the ‘360 patent leaves it to the operator to decide how he or she will select an ROI, and as a result “different operators could select different methods of selecting the region of interest.” (*Id.* at 108:18-109:10.) Siemens’ experts and the literature in the field also confirm that there is no single agreed way in the field for selecting an ROI.

On the second question, the sample ROI selections performed by the experts in this case, including those by Dr. Filler (who is a named inventor on the ‘360 patent and provided an expert report on conspicuity), show that ROI selection substantially affects conspicuity measurements. As a result, not only does the conspicuity measurement depend on who makes the measurement, but it also varies substantially

¹ The Exhibits referenced herein are cited as "IND__" to distinguish the exhibit numbers for this indefiniteness brief from other simultaneous briefing.

even when the very same person of skill in the art (including Dr. Filler) tries to measure the conspicuity of the same tissue twice. Literature in the field also confirms that ROI selection makes a substantial difference in measurements.

Simply put, neither the ‘360 patent nor any agreed standard prescribes a way of selecting ROIs that will lead to objective and reproducible conspicuity measurements. Thus, a person of skill in the art cannot determine whether certain acts are within the scope of the claims or not. The Federal Circuit has held that the existence of that sort of “conundrum” “ends the inquiry” – the claims are indefinite. *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1340 (Fed. Cir. 2003); *see also Geneva Pharms., Inc. v. Glaxosmithkline PLC*, 349 F.3d 1373, 1384 (Fed. Cir. 2003) (“One of ordinary skill would not know from one [situation to the next whether he or she is] within the claim scope or not. That is the epitome of indefiniteness.”).

I. BACKGROUND

A. The Court’s Previous Consideration of the “Conspicuity” Term in This Case

Claims 1 through 35 in the ‘360 patent recite methods for using magnetic resonance imaging (“MRI”) to generate images of a patient. All 35 of those claims incorporate a limitation requiring that the method results in an image where nerve tissue is enhanced compared to other tissue, such that there is “a conspicuity of the nerve that is at least 1.1 times that of [the]/[any adjacent] non-neural tissue.” Even if the ‘360 patent describes a formula for calculating conspicuity,² the conspicuity values

² For purposes of this brief only, Siemens has applied the conspicuity equation Plaintiffs proposed during claim construction, i.e., conspicuity is the mean signal intensity in some nerve ROI divided by the mean signal intensity in some non-nerve ROI ($S_{\text{nerve}}/S_{\text{non-nerve}}$). But Siemens maintains, as explained in its claim construction briefs (D.I. 106 at 11-17; D.I. 108 at 5-9), and as further explained in Dr. Bryan’s Expert Reports (Ex. IND2 (“Bryan Opening Rep.”) ¶¶13-17; Ex. IND3 (“Bryan Rebuttal Rep.”) ¶¶13-17), that the ’360 patent does not adequately identify $S_{\text{nerve}}/S_{\text{non-nerve}}$ as the way of calculating “conspicuity” and that the claims are indefinite for that separate reason.

1 differ depending on the particular regions of interest (“ROIs”) selected for the nerve
2 and non-neural tissue in an MR image.
3

4 Siemens contends that the “conspicuity” limitation in claims 1 through 35 is
5 indefinite under 35 U.S.C. §112, ¶2, because, among other reasons, there is no
6 objective anchor for selecting the ROIs necessary for calculating conspicuity and,
7 therefore, infringement would turn on the subjective choices of the operator who
8 selects the ROIs. (*See, e.g.*, D.I. 108 at 8-9.) In its claim construction order, the Court
9 noted this argument was “very persuasive,” but deferred ruling on this issue in light of
10 some questions the Court found unresolved by the claim construction briefing,
11 including: (1) do persons of skill in the art “agree[] on a method of making [ROI]
12 selections”; and (2) do differences in ROI selection mean that “infringement would
13 depend on who makes the measurement?” (D.I. 114 at 14-15.) The Court has thus
14 permitted the parties to provide additional expert testimony and briefing on these
15 issues. (*Id.* at 15.) The record now confirms that there is no agreed method for
16 selecting ROIs and infringement depends on who makes the measurement. (*See infra*
17 sections III.A-III.B.)

18 **B. Conspicuity Calculations Provided by Experts in This Case**

19 During claim construction, Siemens submitted an expert report from Dr.
20 Michael Moseley showing how a person of skill in the art could select ROIs in the
21 context of the ‘360 patent, and what the resulting conspicuity would be. (*See, e.g.*, Ex.
22 IND4, Ex. C to Moseley Opening Rep.) Plaintiffs submitted a rebuttal report from Dr.
23 Aaron Filler (who is a named inventor on the ‘360 patent and the CEO of Plaintiff
24 NeuroGrafix), which also shows examples of ROI selections and resulting conspicuity
25 calculations. (*See, e.g.*, Ex. IND5, Ex. A to Filler Rebuttal Rep.) The images Dr.
26 Filler used in his report are images Plaintiffs contend were made using a method that
27 infringes the ‘360 patent. (*See, e.g.*, Ex. IND6, Filler Rebuttal Rep. ¶48; D.I. 107 at
28 8.)

1 After the Court's claim construction order, both parties engaged new experts to
2 address the specific issues raised in the Court's claim construction order. Siemens'
3 expert, Dr. Nick Bryan, M.D., PhD, is the Chairman of Radiology at the University of
4 Pennsylvania and specializes in neuroradiology. (Ex. IND2, Bryan Opening Rep. ¶¶4-
5 7.) Dr. Bryan's report shows his own ROI selections and conspicuity calculations
6 using the same data files (referred to as "DICOM" data files) that Dr. Filler used in his
7 rebuttal report. (*Id.* at 15 n.3; Ex. IND12, Ex. C to Bryan Opening Rep.) Dr. Bryan's
8 analysis shows that the conspicuity calculation, and therefore infringement, depends
9 on who makes the measurement and on precisely how they select their ROIs. (*See*
10 *infra* section III.A.) As explained *infra*, section III.B, Dr. Moseley's, Dr. Filler's, and
11 Dr. Bryan's results show that ROI selection substantially affects conspicuity
12 measurements.
13

14 Plaintiffs' second expert, Dr. Brant-Zawadzki, did not perform any ROI
15 selections nor did he submit any conspicuity calculations. In fact, he has never –
16 neither during this case nor before it – selected a region of interest or measured the
17 intensity of any of the nerves covered by the claims at issue, i.e., peripheral,
18 autonomic, or cranial nerves three through twelve. (Ex. IND1, Brant-Zawadzki Dep.
19 Tr. at 23:18-24:7; 28:1-22.)³

20 **II. APPLICABLE LEGAL PRINCIPLES**

21 "Because claims [in a patent] delineate the patentee's right to exclude, [35
22 U.S.C. §112, ¶2] requires that the scope of the claims be sufficiently definite to inform
23 the public of the bounds of the protected invention Otherwise, competitors
24 cannot avoid infringement, defeating the public notice function of patent claims."

25

³ Plaintiffs' counsel argued at the claim construction hearing that taking a region of
26 interest of two tissues to determine the contrast between the tissues is "the most basic
27 measurement that radiologists do with MRI." But the experts have confirmed that this
28 is not so — indeed, as Plaintiffs' own expert admits that he has "never done that."
(*Compare* Ex. IND7, 3/24/2011 Hr'g Tr. at 71:11-16, *with* Ex. IND1, Brant-Zawadzki
Dep. Tr. at 28:11-22.)

1 *Halliburton Energy Servs., Inc. v. M-I LLC*, 514 F.3d 1244, 1249 (Fed. Cir. 2008);
2 *Morton Int'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470 (Fed. Cir. 1993) (claims
3 must be “sufficiently precise to permit a potential competitor to determine whether or
4 not he is infringing”). The “determination of claim indefiniteness is a legal conclusion
5 that is drawn from the court’s performance of its duty as the construer of patent
6 claims.” *Exxon Research & Eng’g Co. v. United States*, 265 F.3d 1371, 1376 (Fed.
7 Cir. 2001). In performing that duty and evaluating indefiniteness, “a court may
8 consider or reject certain extrinsic evidence in resolving disputes en route to
9 pronouncing the meaning of claim language.” *Id.*

10 **III. ARGUMENT: THE “CONSPICUITY” TERM IN CLAIMS 1 THROUGH
11 35 RENDERS THOSE CLAIMS INDEFINITE.**

12 Patent law requires patent claims to have “an objective anchor” that “allow[s]
13 the public to determine the scope of the claimed invention.” *Datamize, LLC v.
14 Plumtree Software, Inc.*, 417 F.3d 1342, 1350 (Fed. Cir. 2005). As the expert reports
15 in this case and the literature in the field demonstrate, drawing an ROI is neither
16 objective nor reproducible. In particular, as explained in the following subsections:

- 17 (A) the ‘360 patent fails to identify the single way by which ROIs should be
18 selected (let alone a precise protocol that would be reproducible);
- 19 (B) there is no agreed standard in the field for selecting ROIs;
- 20 (C) even slightly different ROIs lead to substantially different signal intensity
21 measurements, and even the various methods described in the literature
22 do not necessarily lead to reproducible ROI selections; and,
- 23 (D) as a result of (A), (B), and (C), an infringement determination will
24 depend on who draws the ROIs and precisely how they draw them.

25 The inescapable consequence is that claims 1 through 35 are indefinite, because an
26 operator cannot know with any reasonable certainty whether or not he is within the
27 scope of the claims. *Morton Int'l*, 5 F.3d at 1470 (holding claims indefinite because
28 they were “not sufficiently precise to permit a potential competitor to determine

whether or not he is infringing"); *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d at 1340-42 (claim indefinite: although the patent referenced multiple ways of determining the baseline for the claimed glycosylation differences, "the patent failed to identify a **single standard** by which the 'difference' could be measured" and the literature in the field showed that two different uEPO samples, "though produced by the **same procedure . . . ,** [could] nonetheless ha[ve] different glycosylation");⁴ *Geneva Pharms.*, 349 F.3d at 1384 ("[O]ne of skill would not know from one [situation to the next whether they are] within the claim scope or not. That is the epitome of indefiniteness.").

The definiteness requirement is especially important where, like here, the claim limitation in question was critical for patentability. Plaintiffs do not dispute that most – if not all – of the steps in claims 1 through 35 were shown in the prior art before the '360 patent. (D.I. 126.) Rather, in front of the Patent Office and this Court, the patentee has stressed that the key distinction over the prior art was achieving a conspicuity of 1.1. (See, e.g., D.I. 107 at 3 (conspicuity requirement "was a significant basis for distinguishing the prior art"); JA96; JA131-32; JA151; JA173.) Under these circumstances, failure to provide a definite scope for the conspicuity term is fatal to the claims. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1218 (Fed. Cir. 1991) ("When the meaning of claims is in doubt, especially when, as is the case here, there is close prior art, they are properly declared invalid."); see *Halliburton*, 514 F.3d at 1253 ("Halliburton's failure to distinguish the fragileness of the drilling fluids of the invention from the close prior art . . . is fatal.").

With this background, the following subsections address the questions raised by the Court's claim construction order.

⁴ All emphasis added unless otherwise noted.

1 **A. Persons of Skill in the Art Reading the ‘360 Patent Will Select**
2 **Different ROIs**

3 **1. The ‘360 Patent Does Not Prescribe a Single Method for**
4 **Selecting ROIs**

5 The ‘360 patent fails to prescribe the single way an operator should select the
6 ROIs used in the “conspicuity” calculation. Rather, the ‘360 patent merely notes that
7 there are several general approaches for ROI selection. (‘360 patent, 14:54-62, 27:65-
8 28:26 (noting an ROI can be a “single pixel or voxel” or alternatively an undefined
9 “larger region”; “ROI selection can be performed manually using, for example, a
10 keyboard or mouse to move a cursor” or, “[a]lternatively, ROI selection may be
11 accomplished automatically via a sequential selection of all pixels or via an external
12 input regarding a particular region from, for example, diagnostic system 24”;
13 “thresholding” could also be used).) Nowhere does the patent sufficiently prescribe
14 an objective or repeatable protocol for ROI selection, and even the choice between the
15 high-level approaches mentioned in the patent is left entirely to the operator. (Ex.
16 IND2, Bryan Opening Rep. ¶35 (“[N]othing in the ‘360 patent itself or the prosecution
17 history indicates the precise method for selecting the appropriate ROI for the
18 conspicuity calculation required by the claims. Rather, the ‘360 patent simply leaves
19 open the possibility of using any method of selecting an ROI, of which there are
many.”).)

20 Indeed, Plaintiffs’ expert concedes that the ‘360 patent suggests at least three
21 different ways of selecting an ROI, that the patent leaves the choice among them
22 entirely to the operator, and that different operators reading the ‘360 patent could
23 therefore choose different methods:

24 Q. And the patent itself says it can be one of a host of different
25 ways of selecting a region of interest; correct?

26 A. It gives examples of three, I guess, right there.

27 *****
28

1 Q. It doesn't say which of those is the right one to use or which
2 of those to use to determine conspicuity; correct? It leaves
3 that up to the operator?

4 A. Right.

5 Q. And you'd agree with me that different operators could
6 select different methods of selecting the region of interest?

7 A. Yes.

(Ex. IND1, Brant-Zawadzki Dep. Tr. at 108:18-22; 109:2-10; *see also id.* at 127:8-128:3 ('360 patent does not provide "one standard way" to select an ROI).) Thus, the '360 patent fails to identify exactly how ROIs should be selected. *See Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d at 1341 (finding claim indefinite where "district court concluded that the patent failed to identify a **single standard** by which the [claimed] 'difference' could be measured"); *Union Pac. Res. Co. v. Chesapeake Energy Corp.*, 236 F.3d 684, 692 (Fed. Cir. 2001) (holding claimed "comparing" indefinite because it "presumably refers to a complex 'correlation' step suggested (but not explained) in the written description").⁵

16 **2. There Is No Agreed Standard that Persons of Skill in the Art
17 Use for Selecting ROIs**

18 Because the '360 patent does not sufficiently prescribe a specific ROI selection
19 protocol, Plaintiffs have argued that a person of skill in the art simply "would have
20 known how to determine an appropriate ROI." (D.I. 107, at 6.) The scope of the
21 patent claims cannot, however, rely solely on the bare assertion that a person of skill
22 in the art "would know how to" determine the scope of a claim limitation when the
23 patent itself wholly fails to disclose the scope. *See D.I. 114* (Claim Construction
24 Order) at 15 (noting Plaintiffs' assertion that persons of skill in the art will have "great
25 experience at . . . selecting [an ROI]" "is problematic because NeuroGrafix failed to

26

⁵ *See also Arcade Inc. v. 3M Co.*, 24 U.S.P.Q.2d 1578, 1587 (E.D. Tenn. 1991) (claim
27 indefinite: "Nowhere does the '299 patent specify what tests are to be run to ascertain
28 that tensile rupture strength. There are various speeds at which tests may be run
 which could make a difference in test results.").

1 identify supporting evidence for it"); *In re Frederiksen*, 213 F.2d 547, 548 (C.C.P.A.
2 1954) ("Since the specification fails to disclose the metes and bounds of the operative
3 proportions either generally or specifically, that deficiency is not supplied or corrected
4 by the contention that those skilled in the art would know what the maximum or
5 optimum amounts would be."); *S.O.I.TEC Silicon On Insulator Techs. v. MEMC Elec.*
6 *Materials, Inc.*, 745 F. Supp. 2d 489, 508-09 (D. Del. 2010) ("Even assuming that
7 these post-anneal tests (1) are accurate and (2) did not destroy the substrate . . . , this
8 technique does not appear in the [asserted] patents, and cannot be used to satisfy §
9 112.").
10

11 And here, contrary to Plaintiffs' unsupported assertion, the evidence shows that
12 "***there is no recognized standard for selecting an ROI.***" (Ex. IND2, Bryan Opening
13 Rep. ¶31.) Indeed, Plaintiffs' expert admits that "***there's no industry standard one***
14 ***way of*** ***selecting ROIs.***⁶ (Ex. IND1, Brant-Zawadzki Dep. Tr. at 126:17-128:3.)

15 Beyond the experts in this case, other scientists in the field similarly recognize
16 that there is no agreed method for ROI selection, and to mitigate the inherent
17 variability in ROI selections they explain in each study exactly how their ROIs were
18 selected. For example, an article by S. Biswas et al. prescribes the precise size, shape,
19 and placement of ROIs used in that particular study, in order "to reduce the
20 variability" in the results:

21 ROIs were positioned in the genu of the corpus callosum (GCC),
22 speñnium of the corpus callosum (SCC), right and left anterior
23 internal capsule (AIC). . . . The ROIs were placed exclusively
24 within the central portion of the visualized white matter tracts and
25 the right thalamus, and on the middle section if the structure was
seen on 3 adjacent sections. The ROIs were 0.05 cm² (in the
internal capsules and corticospinal tracts) and 0.20 cm² (in the

26 ⁶ Although Plaintiffs' expert agrees there is no industry standard, his view is that
27 "most people would do it the way [Siemens' expert, Dr. Bryan,] did it." (Ex. IND1,
28 Brant-Zawadzki Dep. Tr. at 126:21-127:7.) As discussed, *infra* section III.B, the way
Dr. Bryan and Dr. Filler did it in their reports leads to utter uncertainty about whether
the conspicuity limitation is met in a particular case.

1 corpus callosum and thalamus) and were identical between the 2
2 sessions to reduce the variability accounting for the validity of the
3 results (Fig 1).

4 (Ex. IND8, at 1129.) Other articles similarly describe precisely how the operators
5 selected ROIs, and in some studies the authors provide the operators with a “template”
6 for ROI selection.⁷

7 Plaintiffs’ expert acknowledges this practice in the field – the practice of
8 precisely prescribing the ROI protocol for each particular study – and he explains that
9 ***this practice is “for the purposes of reproducibility by another researcher.”*** (Ex.
10 IND1, Brant-Zawadzki Dep. Tr. at 53:15-54:4; *see also id.* at 54:4-10 (“[Y]es, people
11 in publications often describe the [ROI] methodology because that’s an important part
12 of publishing a paper is for other researchers to understand how that particular set did
13 it and limitations of that, if any, and its ability to be reproduced.”). Plaintiffs’ expert
14 also admits that the ‘360 patent could have provided the level of detail shown in the
15 literature, but that the patent simply does not do so.

16 Q. You agree there are more specific ways to prescribe how to
17 select an ROI than what’s set forth in this patent?

18 A. Can you be much more prescriptive about how to select an
19 ROI? Can you say -- yes, you should only use an ROI that’s
20 three pixel by three pixel and that’s it. You can be more
specific in prescribing how, for a given purpose to determine
an ROI, but that’s -- okay. That’s my answer.

21 ***

22
23
24 ⁷ See, e.g., Ex. IND9, at 4, fig.2 (“The size of the ellipsoid ROIs was chosen to
25 encompass 16 pixels (from interpolated data to a 256x256 matrix)” and “placed on
26 one single fiber tract cross-section” including the “cerebral peduncle (2), anterior limb
27 of the internal capsule”); Ex. IND10, at 1520 (listing specific ROI protocols,
28 such as “maximum pixel value only” and “15 x 15 mm square ROI centered on the
location of maximum pixel value”); Ex. IND11, at 294-95 (listing specific ROI
protocols, such as “[c]ircular 15-mm-diameter ROIs were drawn semi-automatically
over the area of maximum FDG uptake in a lesion”).

1 Q. *And the '360 patent does not provide [the level of detail*
2 *found in a published article] for the ROI selection.*
3 *Agreed?*

4 A. That's not the purpose of the patent.

5 Q. I didn't ask you what the purpose was, sir. I asked you if it
6 described it or not?

7 A. *It does not.*

8 (Ex. IND1, Brant-Zawadzki Dep. Tr. at 170:13-22; 171:24-172:5; Ex. IND3, Bryan
9 Rebuttal Rep. ¶52.) Thus, in failing to provide sufficient details on how to select
10 ROIs, the '360 patent does not even adhere to the practice in the field that would have
11 allowed at least some level of reproducibility. *Frederiksen*, 213 F.2d at 547-48
12 (affirming indefiniteness where “it has been the uniform practice in the art . . . to
13 define the amount of precursor used,” but the patent application failed to define the
14 amount of precursor in the claimed invention).

15 Without a prescribed method for selecting ROIs, each operator is left to come
16 up with his or her own ROI selection protocol and to make myriad choices in doing
17 so. As explained below, ROI selection substantially affects signal intensity
18 measurements and, in turn, conspicuity calculations. Operators are therefore left with
19 no repeatable or objective way of measuring conspicuity to determine whether they
20 have met the conspicuity requirement in claims 1 through 35.

21 B. **The Infringement Determination for Claims 1 through 35 Depends
22 on ROI Selection**

23 1. **ROI Selection Substantially Affects the Signal Intensity
24 Measurements Used for Calculating Conspicuity**

25 The sample ROI selections and corresponding signal intensity measurements
26 performed by the experts in this case, including those by co-inventor Dr. Filler, show
27 that ROI selection *substantially* affects the measured signal intensity of a tissue.
28 *Honeywell Int'l, Inc. v. Int'l Trade Comm'n*, 341 F.3d 1332, 1341 (Fed. Cir. 2003)
29 (claim indefinite because “the different sample preparation methods do not produce
30 identical or even ‘essentially identical results.’”).

1 Dr. Bryan selected ROIs in several images that Plaintiffs contend were made
2 using steps that infringe the ‘360 patent, and concluded that the measured intensity of
3 a tissue varies substantially depending on the size, shape, and position of the ROI in
4 the tissue. (Ex. IND2, Bryan Opening Rep. ¶¶41, 46-53.) As just one example, Dr.
5 Bryan’s analysis demonstrates that the measured intensity of a nerve in one image
6 varied by approximately 60% depending only on the size and position of the ROI.
7 (Ex. IND12, Ex. C to Bryan Opening Rep. fig.8 (intensity varies from 72.0 to 112.5
8 for the same nerve in ROI Nos. 6 through 10). The measured intensity of non-neural
9 tissue similarly varies depending on the size and position of the ROI, and also varies
10 depending on which type of non-neural tissue the operator chooses to include in the
11 background. (*Id.* fig.9 (non-neural tissue intensity varies from 56.0 to 100.5).)
12

13 Dr. Filler’s report shows that even when the same operator (Dr. Filler himself)
14 tries to select an appropriate ROI on the same tissue twice, the signal intensity
15 measurements vary substantially. For instance, figures 5, 6, and 7 in Exhibit A to Dr.
16 Filler’s rebuttal report show a series of conspicuity measurements Dr. Filler performed
17 on the same MR image. (Ex. IND5, Ex. A to Filler Rebuttal Rep. figs. 5, 6, 7.) In
18 each figure, Dr. Filler selected an ROI to measure the signal intensity of the same non-
19 neural tissue (lung tissue). Dr. Filler acknowledges the resulting measurements vary
20 based on what he characterizes as “slightly different” ROIs. (Ex. IND6, Filler
21 Rebuttal Rep. at 17 n.5.) But those “slightly different” ROIs lead to more than 40%
22 variation in the resulting intensity measurements – a substantial variation, not a
23 “slight” variation. (Ex. IND5, Ex. A to Filler Rebuttal Rep. figs. 5, 6, 7 (mean
24 intensity of lung measured as 13.77, 16.76, and 19.32, respectively); *see also id.* figs.
25 4, 5, 6, 7 (variation in the mean intensity of plexus nerve tissue).)

26 Dr. Moseley likewise showed that ROI selection substantially affects measured
27 intensity. For instance, Dr. Moseley’s sample measurements showed that the intensity
28 for non-neural tissue in one image varied by over 100% depending on how the

operator selected the ROI. (Ex. IND4, Ex. C to Moseley Opening Rep. figs. 2-5 (mean intensity of non-neural tissues measured as 371.782, 571.818, 428.141, and 274.203, respectively).)

Dr. Brant-Zawadzki, Plaintiffs' second expert in this case, has never – neither during this case nor before it – selected a region of interest or measured the intensity of any of the nerves at issue in the claims, i.e., peripheral, autonomic, or cranial nerves three through twelve, and Plaintiffs did not ask him to do so in this case. (Ex. IND1, Brant-Zawadzki Dep. Tr. at 22:21-24:7; 25:21-26:2; 27:2-23; 28:1-22.) To the extent Plaintiffs or their expert contend that the average signal intensity of the ROI will not vary significantly based on the size, shape, or position of the ROI selected, that view is contrary to the results shown in Dr. Bryan's, Dr. Moseley's, and Dr. Filler's reports, as well as by the medical imaging literature, which confirms over and over that the precise ROI selection makes a substantial difference. Indeed, the literature concludes that ROI selection is *not* repeatable without a careful definition of the precise ROI selection protocol, which the '360 patent does not provide.⁸ (See IND3, Bryan Rebuttal Rep. ¶¶46-48.)

⁸ See, e.g., Ex. IND15, at 1126 (finding “pattern of high variability”: “[t]he variability from one observer to the other largely lies in the placement of the ROIs”), 1126 (“rater performance is also an important source of variability,” and “while 2 observers may have equivalent training . . . , delineation of ROIs without the assistance of a template or reliance on single ROIs . . . may introduce sources of error and contribute to data variability.”), 1126 (“We suggest that standardizing and using schemes of ROIs should allow reduction of interobserver and intraobserver variability.”); Ex. IND13, at 101 (“The influence of the operator is very large, as can be seen in the top graphs (ROI dependence.”), 103, 105 (noting that one technique (“MLM”) resulted in error rates of 50%, even though it was characterized as the “best” technique in that study); Ex. IND14, at 200, 202 (ROI computations “suffer from significant inter- and intraobserver variations in the computed volumes”); Ex. IND8, at 1132 (“[A]s pointed out by other researchers, the interobserver variability, which may be 3 times higher than the intraobserver variability, remains a serious problem in the interpretation of the FA maps. A voxelwise analysis, compared with a ROI-based analysis, may seem attractive to eliminate operator-dependent ROI misplacement, partial volume averaging, and interobserver or intraobserver variability”); Ex. IND9, at 8 (“FA findings are potentially more difficult to compare due to potential variability and errors associated with ROI placement.”), 9 (“the only operator dependent step in the

Where, as here, a patent claim leaves potential infringers the choice among different methods to determine the scope of the claim, and the methods produce different results, the claim is indefinite. *Honeywell*, 341 F.3d at 1341 (claim limitation requiring certain melting point elevation (“MPE”) indefinite because the published methods for determining MPE did not “produce identical or even ‘essentially identical results’”); *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d at 1341.

2. Persons of Skill in the Art Will Reach Different Conclusions as to Whether the “Conspicuity” Term is Met Depending on Their ROI Selections

Plaintiffs have argued that even if ROI selection affects signal intensity measurements, it somehow does not “affect the outcome” of the infringement analysis. (D.I. 107, at 7.) But in light of the substantial effect ROI selection has on signal intensity measurements for the nerve and non-neural tissue, it is logically and mathematically inescapable that ROI selection has a substantial effect on any ratio of those intensities (i.e., conspicuity). (See Ex. IND2, Bryan Opening Rep. Ex. ¶¶30-35; IND3, Bryan Rebuttal Rep. ¶¶45-48.) Dr. Bryan’s and Dr. Filler’s sample conspicuity calculations confirm what logic dictates – ROI selection substantially affects the determination of whether the conspicuity limitation is met. Whereas one set of ROIs might show infringement, a different set of ROIs will show non-infringement. And with no objective standard for ROI selection specified in the patent or in the field, there is no objective or rational basis for choosing between the different sets of ROIs. *Datamize*, 417 F.3d at 1350 (“Some objective standard must be provided in order to allow the public to determine the scope of the claimed invention.”).

intra-rater and inter-rater analyses was the subjective placement of the ROIs”); *see also* Ex. IND2, Bryan Opening Rep. ¶¶30-35 (quoting articles that concludes that “a standardized method of ROI selection and analysis of dynamic breast MR data is yet to be established” and that the “method of ROI definition has a direct influence on quantitative outcome”).

Using the same MR image data that Dr. Filler used in his report, Dr. Bryan's report demonstrates that ROI selection "substantially impacts . . . the ultimate conspicuity measurement."⁹ (Ex. IND2, Bryan Opening Rep. ¶30; *see also id.* ¶¶49, 53.) As an example, while Dr. Filler calculated the conspicuity of a particular nerve as ***greater than 1.1*** in a particular image, Dr. Bryan's report shows that slightly different ROI combinations in the same tissues in the same image result in conspicuity values of ***less than 1.1***. (*Compare* Ex. IND5, Ex. A to Filler Rebuttal Rep. fig.3 (calculating conspicuity of C7 spinal nerve compared to scalene muscle as 1.40), *with* Ex. IND12, Ex. C to Bryan Opening Rep. tbl.6 (calculating conspicuity of C7 spinal nerve compared to scalene muscle as less than 1.1, and as low as 0.97); *see also* Ex. IND2, Bryan Opening Rep. ¶43 ("There is no basis in the patent or the knowledge of a person of ordinary skill in the art to select the ROIs Dr. Filler used instead of other ROIs that show a conspicuity of less than 1.1.").) Thus, the infringement determination changes depending on who measures the conspicuity of an image. (*See* D.I. 114 (Claim Construction Order) at 15 (noting the indefiniteness "problem" if "infringement would depend on who makes the measurement")); *see also Baldwin Graphic Sys., Inc. v. Siebert, Inc.*, 2008 WL 4083145, at *8-9 (N.D. Ill. Aug. 27, 2008) (claims indefinite: "The first calculation may result in a product that infringes on the patent, while the second may not. Which is correct? From the claims, specification and preferred embodiment we cannot say.").

As another example, Dr. Filler's report demonstrates that even Dr. Filler himself may reach opposite conclusions about whether the conspicuity limitation is met when he tries to reproduce his own conspicuity measurements. Figures 5, 6, and 7 in Exhibit A to Dr. Filler's report show a series of measurements performed on the

⁹ Dr. Moseley likewise concluded based on his calculations and experience that "[t]he measured or calculated conspicuity would . . . differ greatly depending on the subjective determination of which portion or portions of the structure to assess . . . and how the region of interest is selected." (Ex. IND16, Moseley Opening Rep. ¶33.)

1 same MR image, and in each figure Dr. Filler selected ROIs to calculate the
2 conspicuity of plexus nerve tissue compared to lung tissue. Claim 19 of the '360
3 patent requires conspicuity of greater than 5,¹⁰ and based on the "slightly different"
4 ROIs used in figures 5, 6, and 7, (Ex. IND6, Filler Rebuttal Rep. at 17 n.5), Dr.
5 Filler's conspicuity calculations show that a person of skill in the art **could equally**
6 **conclude that the conspicuity requirement in claim 19 is met** (conspicuity of greater
7 than 5 in figure 5) **or not met** (conspicuity of less than 5 in figures 6 and 7,
8 respectively). As Dr. Brant-Zawadzki explained Dr. Filler's conspicuity results:
9

10 Q. So at least with respect to this image, when Dr. Filler
11 himself used three different settings on the DICOM data and
12 three different ROIs. One of them fell over the five
limitation of claim 19 and two of them fell below that; right?
13 A. Over or under, yes.

14 Q. The same data, the same scan, depending on how you
15 measured it, would satisfy the [claim 19] limitation or not
satisfy it depending on the [ROI] selection; true?

16 A. Yes.

17 Q. That's what this shows?

A. Yes. It speaks for itself.

18 (Ex. IND1, Brant-Zawadzki Dep. Tr. at 188:14-189:2; *see also id.* at 182:20-188:20
19 (discussing figures 5, 6, and 7 from Exhibit A to Dr. Filler's Rebuttal Rep.; *see Ex.*
20 IND5). "The inability of the expert [Dr. Filler] to use the parameters he himself
21 identified to determine whether [the claim limitation was met] militates against the
22 reasonableness of those parameters as delineating the metes and bounds of the
23 invention." *Datamize*, 417 F.3d at 1354.

24
25 ¹⁰ Claim 19 requires that the image shows "the nerve at an intensity of at least 5 times
26 that of the non-neural tissue." The parties agree that, under Plaintiffs' proposed
27 construction of "conspicuity," the intensity limitation in claim 19 should be
understood the same as the conspicuity limitation in the other claims, such that claim
28 19 effectively requires a "conspicuity of the nerve that is at least 5 times that of the
non-neural tissue." (See Ex. IND6, Filler Rebuttal Rep. ¶13; D.I. 113-A at 48
(NeuroGrafix's Proposed First Amended Infringement Contentions).)

These results show that persons of skill in the art will reach different conclusions about infringement depending on how they select their ROIs, and potential infringers cannot therefore reasonably determine whether or not the conspicuity limitation is met. Under these circumstances, the claims are indefinite. *Morton Int'l*, 5 F.3d at 1470 (claims indefinite because they “are not sufficiently precise to permit a potential competitor to determine whether or not he is infringing”); *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d at 1342 (finding claim indefinite because patent “does not direct those of ordinary skill in the art to a standard by which the [claimed] comparison can be made”); *Geneva Pharms.*, 349 F.3d at 1384 (“One of ordinary skill would not know from one [situation to the next whether they are] within the claim scope or not. That is the epitome of indefiniteness.”); *Baldwin Graphic Sys*, 2008 WL 4083145 at *8-9 (“Defendant’s experts may have no trouble determining that a product does not infringe, while plaintiffs’ expert may have no trouble determining that the same product infringes. Without a reference standard [in the patent], we have no choice but to determine that independent claims 1 and 14, along with their respective dependent claims, are ‘insolubly ambiguous’ and therefore invalid.”); *Duplan Corp. v. Deering Milliken, Inc.*, 444 F. Supp. 648, 738 (D. S.C. 1977) (“The patentee simply failed to inform the public of the limits of his monopoly with the result that those producing the yarns could never know which processes could be safely used without a license and which could not.”; “The patent law does not require alleged infringers to play this type of Russian roulette.”), *aff'd in part, rev'd in part on other grounds*, 594 F.2d 979 (4th Cir. 1979).

IV. CONCLUSION

For these reasons, Siemens respectfully requests the Court grant summary judgment of invalidity dismissing claims 1, 3, 7, 11, 12, 18, and all asserted claims dependent upon those claims, as indefinite.

1
2 DATED: August 24, 2011
3

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on August 24, 2011, a copy of the foregoing MEMORANDUM IN SUPPORT OF SIEMENS' MOTION FOR PARTIAL SUMMARY JUDGMENT OF INVALIDITY BASED ON INDEFINITENESS OF "CONSPICUITY" IN CLAIMS 1, 3, 7, 11, 12, 18, AND THEIR ASSERTED DEPENDENT CLAIMS IN 5,560,360 was served upon counsel of record for Plaintiffs registered with the Court's CM/ECF system.

/s/Sean M. McEldowney